rhinotracheitis" and "coccidiosis" (a major disease of poultry and swine), respectively. The present amendment corrects the spelling of Feline rhinotracheitis in Claim 3. The amendment also corrects the spelling of the disease coccidiosis, along with *Serpulina pilosicoli* and Turkey rhinotracheitis, in the specification on page 8, lines 24-26. However, it was realized that since a protozoan agent causes coccidiosis, the use of the term in Claim 3 would not find proper antecedent basis in the bacterial or viral antigen of Claim 1. For this reason, a new Claim 31 is presented that is drawn to the method of providing protection against the disease of coccidiosis. Support for the claim is found in original Claim 3 and the specification on page 8, lines 24-26.

The Advisory action of 09/07/2005 states that the previous amendment raised new issues and required further consideration or search. Contrary to the Office opinion, Applicants feel that the amended claims responded directly to the Examiner's own comments in support of her final rejection. The claims, if amended as previously proposed to include 'wherein the presence of the flavorant improves protection against the disease by inducing increased intake of the vaccine by the animal,' did not present any issue that had not been originally acknowledged by the Examiner. In the 06/01/2005 Office action, the Examiner mentions that the instant claims did not include the limitation of "how to moderate or improve the amount of vaccine formulation that the bird will consume" on page 7; and "the method claimed in the instant claims is not required to provide 'improved results' or 'significant 100% protection'" on page 10. By making such statements, the Examiner could expect that Applicants would respond in kind. It is reasonable to presume that the amendment, as previously made, might work to overcome the cited primary references of Brinton *et al.* and Bricker *et al.*, each in view of Strobel *et al.* and Collins *et al.* By presenting the amendment, Applicants had attempted in good faith to conform the claimed invention to the Examiner's inference of patentable subject matter. It is logical to conclude, therefore, that the amendment did not raise new issues and could have been entered in the record.

In terms of the new matter rejection, it has never been the Office practice to require that the support for amendments in the specification need to be taken literally, word for word. See, for example, the guidelines in M.P.E.P. § 2163.07 that state that rephrasing or rewording of a passage where the same meaning remains intact does not constitute new matter. The application teaches in Example 2 on page 30, lines 23-28, that the flavored orally administered vaccine of the invention provided "greater protection against infection as compared to unflavored"

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meaning, quite simply, that 'the flavorant improves protection' as written in the amendment that was not entered. Despite the belief that the phrase does not embrace new subject matter and the meaning of the phrase has been adequately disclosed in the specification, Applicants are currently providing precise language in the present amendment that is consistent with the exact wording used on page 30, lines 23-24 and page 3, lines 12-13 in the specification in order to permit the Examiner to enter this amendment in the record without hesitation. Nevertheless, it should be appreciated that Applicants have been making their best efforts to advance prosecution towards allowance right from the start.

For the foregoing reasons, it is respectfully asked that the Examiner now enter and consider the proposed amendment albeit after a final rejection. The amendment adds no new matter and requires only a cursory review by the Examiner. For the convenience of the Office staff, the amendment is placed in the below Appendix and incorporated herein by reference thereto.

There has been a long-standing but unresolved need recognized in the veterinary field to avoid animals' rejection of oral vaccines and permit effective mass vaccination of animals in a short period of time. Solving the long-felt problem, the present method improves mass vaccination and the protection of animals against disease through the addition of a critical component, namely, the water-soluble flavorants, to oral vaccines. Applicants discovered that, surprisingly, the addition of flavorants significantly improved the likelihood of successful administration and intake of oral veterinary vaccines. Quite beneficially, the improved oral method of mass vaccination of animals reduces the costs of individual administration, the stress and the meat damage that often occur with traditional parenteral vaccination programs. In addition, the present invention achieves successful oral vaccination of animals by providing improved compliance of animals to self-administer sufficient amounts of oral vaccine compositions, eliminating rejection (spitting out) of the oral vaccine and inducing increased intake of the vaccine.

To summarize Applicants' position for the benefit of the Examiner, the following reasons validate allowance of the present patent application:

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(1) The collective art, taken as a whole, totally fails to teach or suggest the claimed method and any reasonable expectation of success.

It cannot be ignored that Strobel *et al.* effectively teaches away from the invention in regard to a significant component of the claimed method. Patentees teach that it is the artificial sweetener that enhances the palatability of the hydroxyacylated amoxicillin solution. There is no inference that flavorant alone will enhance the palatability of the hydroxyacylated amoxicillin solution to pigs. Based on the reference's express showing, one of ordinary skill in the art would at best only predict that an artificial sweetener (or sugar) will improve self-administration of antibiotics to an animal such as a pig, but clearly not a flavorant (*i.e.*, instant Claim 1), and most definitely not a flavorant used in mass vaccination of numerous animals (*i.e.*, instant Claim 7).

Moreover, the art does not teach or imply that an animal will voluntarily swallow an efficacious dose of vaccine formulation that includes flavorant in the absence of sweetener and is administered with a syringe (*i.e.*, instant Claim 10). Roland, for instance, only uses a syringe to administer his vaccine to birds via the art-recognized procedure of oral gavage that is a well-known experimental method for force-feeding drugs to non-compliant animals. One would have no reasonable expectation of success from Roland that one would be able to induce increased intake of the oral vaccine by an animal. In fact, the opposite assumption would be true. Without Roland's force-feeding, one would clearly anticipate that the bird would spit out the vaccine and never get sufficient blood levels for the vaccine to be effective in preventing disease. One of ordinary skill in the art would not assume, based on the state of the art when the application was filed, that an animal would self-administer an oral vaccine to achieve adequate dosing to prevent disease from the bare use of the flavorant alone without inventive effort.

(2) There is no explanation of why the ordinary practitioner would have been motivated, at the time the present invention was made, to make the proposed modification of the applied references that would be necessary to arrive at the claimed subject matter.

To arrive at the claimed subject matter, the ordinary practitioner would need motivation to omit the sweetener of Strobel *et al.* as an indispensable ingredient and resolve other major issues in an attempt to achieve mass vaccination of animals. Since Strobel *et al.* teach that the sweetener is the critical component for enhancing the palatability of their antibiotic solution, it is

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clear that motivation to find the flavorant, herein claimed as the crucial factor in the present method of providing protection against disease, is lacking in the collective art.

Plus, the palatability factor, taken alone, does not automatically guarantee that an oral veterinary vaccine will be self-administered, will be efficacious and will induce the increased intake by animals in sufficient amounts to protect against disease. Adequate dosages, timing and efficacy considerations will differ markedly between, on the one hand, the administration of antibiotics to herds and, on the other, the mass administration of an oral vaccine to animals. What works for antibiotics might not work for oral vaccines, and *vice versa*. Hence, predictability and motivation to make the required change to the teachings of Strobel *et al.* are totally missing from the cited art.

(3) The evidence of superior or unexpected results fully rebuts a *prima facie* case of obviousness.

The working examples demonstrate that the oral vaccination program of the present invention provides superior results from the addition of the palatable flavorant in which the results are both unexpected and significant, *i.e.*, the results are greater than those that would have been expected from the art to an unobvious extent and the results are of a significant, practical advantage. In particular, the Examiner's attention is again drawn to Example 2 (pages 30-32) in which the comparative data demonstrate a remarkable and unexpected difference between the flavored and unflavored vaccine formulations delivered through drinking water (Tables 5 and 6). Upon challenge, a single oral dose of $1x10^7$ of unflavored vaccine gave a mere 10% protection and a single oral dose of $2x10^7$ of the unflavored formulation gave a paltry 22% protection. In sharp contrast, a single oral dosage of $1x10^7$ or 2 oral doses at $1x10^7$ per dose of the flavored formulation provided unexpected and substantially improved protection from disease of 50% and 75%, respectively.

Even more surprisingly, a single oral dose of $5x10^7$ of a strawberry flavored vaccine formulation (containing lyophilized *Erysipelothrix rhusiopathia*) self-administered to the pigs in their drinking water gave significantly improved, 100% effective protection on challenge (Table 4) under circumstances in which the challenged control developed 100% disease. There is no teaching in the collective art to suggest the unexpected and considerably improved results seen

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from the oral, flavored vaccine at the lower dosages or the excellent 100% protection seen at the higher dosages from a self-administered veterinary vaccine formulation in the animals' drinking water. The unforeseen criticality and benefits of the flavorant additive to the oral vaccine formulation of the present invention is neither taught nor suggested by the cited art.

Based on the teachings in the art, one of ordinary skill would not have anticipated the huge success in the mass vaccination of animals as a consequence of the flavorant. Without a doubt, the superior results of the claimed method of the present invention cannot be predicted from the poor results and partial protection obtained by Bricker *et al.* It is clear that none of the collective art teaches how to significantly improve the inadequate and ineffectual protection described by Bricker *et al.*

To conform the claimed method to the showing of the criticality of the flavorant component, the present invention includes the limitation that 'the flavored orally administered vaccine provides greater protection against infection as compared to unflavored' by 'inducing the increased intake of the vaccine by the animal' in exact replication of the wording in the specification on page 30, lines 23-24 and page 3, lines 12-13.

CONCLUDING REMARKS

The further arguments in favor of patentability of the claimed invention that had been made in the last response filed August 23, 2005 that accompanied the non-entered amendment after the final rejection are incorporated herein by reference thereto.

In view of this amendment, the foregoing remarks and the prior remarks of August 23, 2005, Applicants respectfully request that pending Claims 1, 3-10 and 27-31 be held allowable.

The Examiner is encouraged to contact the undersigned attorney to discuss any outstanding issues.

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Accordingly, Applicants believe that this application is in condition for an immediate allowance. Favorable treatment is respectfully urged.

Respectfully submitted,

WYETH

Date: November 1, 2005

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